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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/599,220	06/22/2000	Alfred H. Dougan	4045-0109P	7800

2292 7590 06/18/2002

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EXAMINER

MCGARRY, SEAN

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 06/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/599,220

Applicant(s)

DOUGAN ET AL.

Examiner

Seans McGarry

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3,6,8. 6) ☐ Other:

DETAILED ACTION

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instantly claimed invention is broadly drawn to include any and all oligonucleotides that may bind to any and all proteins that may be a component of a mammalian clotting cascade and also includes any and all proteins that may be bound to the 3' and/or 5' end of the oligonucleotide.

The instant specification discloses two aptamer oligonucleotides that were known in the art at the time of invention (see US 5,756,291, for example) that bind to thrombin where streptavidin or biotin was conjugated to the 3' and/or 5' ends. The disclosure of these two known sequences with biotin or streptavidin conjugated to the 3' and/or 5' end does not allow one in the art to immediately envision the structure of other oligonucleotide aptamers that bind to different proteins that may be a component of a mammalian blood clotting cascade which have been complexed with any protein at the 3' and/or 5' end. The instant disclosure of two species is clearly not representative of the genus instantly embraced in the claims. The members of the genus are highly divergent since each aptamer oligonucleotide varies in sequence and such sequences

are not predicable but must be found de novo for each and every target protein (see US 5,756,291, for example). Each aptamer has different properties. The instant invention is therefore lacking an adequate written description.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffin et al [US 5,756,291], Boado et al [Bioconjugate Chem., Vol. 3:519-523, 1992, cited by applicant].

The instant invention is drawn to a composition comprising a nucleic acid aptamer with a protein conjugated to the 3' and/or 5' end which aptamer binds to a protein that is a member of a mammalian blood clotting cascade and methods of use thereof.

Griffin et al have taught aptamers that bond to thrombin. It has been taught at column 6, for example, that treatment of thrombotic disease is based on inhibition of clotting and/or acceleration of thrombolysis. It has been taught at column 12, for example, that aptamers can be used as a separation means by coupling the aptamer oligonucleotides to a solid support and also that suitably labeled aptamers [such as radioisotopes (see lines 33-44)] can be used in *in vivo* or *in vitro* diagnosis, imaging or histological analysis. It has been taught at columns 17-18, for example that aptamer

Art Unit: 1635

oligonucleotides can contain advantageous modifications to the bases, backbones and sugars of the oligonucleotide. At columns 32-33 it has been taught that in preferred methods separation of the complexes [in separation techniques] any standard coupling agent may be used depending on the nature of the support. At line 19-25 it has been specifically taught the use of biotin and avidin, for example. Examples 6-20 have taught thrombin aptamers and have provided specific teachings for the modification of such oligonucleotide aptamers and further have taught the in vivo use of such aptamers in inhibition of blood clotting. Griffin et al have therefore taught the use of thrombin oligonucleotide aptamers that can be used in separation techniques, diagnostics, imaging, and inhibition of blood clotting in a mammal. Griffin et al have taught that one can modify the oligonucleotides to protect from nucleases, for example (column 18). Griffin et al have taught to label oligonucleotide aptamers with radiolabels, for example. Griffin et al have taught the use of a protein coupled to an aptamer in separation techniques. Griffin et al do not specifically teach the addition of a protein to the 3' and/or 5' end of an oligonucleotide aptamer to inhibit its [the aptamers] degradation.

Boado et al have taught the protection of oligonucleotides against serum nuclease degradation via an avidin-biotin system. It has been taught that such oligonucleotides were biotinylated at the 3' and 5' ends and that the 5' molecules were partially protected and 3' molecule were protected from nuclease attack.

It would have been obvious to make the instantly claimed invention since Griffin et al have provided much teaching on the use of a thrombin specific aptamer for use in the inhibition of blood clotting and has taught that such aptamers can be used in

Art Unit: 1635

imaging, diagnosis with appropriate labels. Since Griffin et al have taught the use of specifically encourage the use modifications to protect aptamers from nuclease protection one in the art would clearly have been motivated to use the avidin-biotin system taught by Boado et al since that system provides protection to oligonucleotides in serum, which one would clearly want in a thrombin specific aptamer.


The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R McGarry whose telephone number is (703)305-7028. The examiner can normally be reached on M-Th (6:00-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SRM
June 17, 2002



SEAN McGARRY
PRIMARY EXAMINER
1635